Equal performance of aspiration and stent retriever thrombectomy in daily stroke treatment

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Abstract

Background

Mechanical thrombectomy with stent retrievers has proven to be safe and effective in endovascular treatment of acute ischemic stroke. Direct aspiration has shown revascularization rates comparable to stent retrievers in the recent ASTER and COMPASS trials, however the efficacy in routine clinical practice has not been shown so far. The aim of our study was to show that aspiration has equal clinical and technical outcomes compared to stent retriever thrombectomy in daily clinical practice.

Methods

We analysed data of patients with a LVO of the anterior circulation registered in the Dutch MR CLEAN Registry between March 2014 and June 2016. Primary outcome was functional outcome measured with the modified Rankin Scale (mRS) score. Secondary outcomes were reperfusion grade, periprocedural complication rate and procedure duration. Association of treatment technique with functional outcome was estimated with univariable and multivariable ordinal logistic regression analysis and expressed as cOR for a shift towards better outcome on the mRS.

Results

As first-line treatment modality, 207 of 1175 patients (17.6%) were treated with direct aspiration, and 968 (82.4%) by stent retriever. We observed no differences in functional outcome (adjusted cOR 1.020 (95% CI 0.68-1.52)) and periprocedural complications. Successful reperfusion (eTICI $\geq$2B) was similar. Duration of the procedure was shorter with aspiration (57 minutes (IQR 35-73) vs. 70 minutes (IQR 47-95), p <0.05).

Conclusion

Direct aspiration shows equal clinical outcomes as stent retriever thrombectomy in our large multicenter real-life cohort. We found no difference in complication rates and shorter procedure times for aspiration.

Introduction

Various recent randomized clinical trials have demonstrated that endovascular treatment (EVT) is safe and effective for patients with acute ischemic stroke with large vessel occlusion (LVO) of the anterior circulation.[1–8] In the vast majority of patients in the intervention arms of these trials, thrombectomy was performed with latest generation thrombectomy devices, so-called stent retrievers.

The alternative technique of contact aspiration thrombectomy as first line treatment has long been debated. Early generation aspiration devices suffered several difficulties, many of which have been overcome by newer generations of large bore flexible catheters.[9–11]

Proposed advantages of aspiration include usability, less injury to vessel wall, shorter procedure times and lower cost.[11–14]

Case series and retrospective single centre data have shown acceptable results.[15] The recently published results of the ASTER trial showed similar revascularization rates for both techniques. ASTER was designed to show superiority of aspiration over stent retriever, but failed to do so. Clinical outcome, assessed as a secondary endpoint, was similar for both techniques.[16] The recently announced but yet to be published results of the COMPASS trial report comparable clinical outcome for both techniques.

The purpose of our study was to compare first line strategy of direct aspiration to stent retriever thrombectomy regarding functional outcome, reperfusion grade, complication rate, and duration of interventional procedure in patients with a proximal arterial occlusion in the anterior circulation in routine clinical practice.

Methods

Design

We analysed differences between groups of patients who were included in the MR CLEAN Registry.[17] The MR CLEAN Registry is a prospective, observational study in all centres that perform EVT in the Netherlands. In this registry, that started following the conclusion of the MR Clean trial on March 16 2014, all patients undergoing EVT (defined as entry into the angiography suite and arterial puncture) are registered. Data about patient characteristics, intervention procedure, complications, reperfusion grade, and clinical outcome are recorded. Data of patients included up to June 15, 2016 are processed and used in this analysis. Sixteen centres participated in the MR CLEAN trial and are considered MR CLEAN centres. Two other centres started performing EVT later on, and their patients were not included in the present study. The MR CLEAN Registry was approved by the medical ethics committee.

Patients

We included patients who underwent first-line treatment with direct aspiration or stent retriever. Patients treated with intra-arterial thrombolysis only, or with a MERCI device or other modality were excluded. Inclusion criteria for this study are age 18 years and older, intracranial proximal arterial occlusion in the anterior circulation (intracranial carotid artery (ICA, ICA-T) or middle (M1/M2) or anterior (A1/A2) cerebral artery) demonstrated by CT angiography (CTA) and arterial puncture within 6.5 hours of symptom onset.[17]

Outcome measures

Primary outcome measure was functional outcome on the modified Rankin Scale (mRS) score at 90 days, ranging from 0 (no symptoms) to 6 (dead). Secondary outcomes were reperfusion grade as according to the extended Thrombolysis in Cerebral Infarction (eTICI) scale score at

end of the intervention procedure, complication rate, and time to reperfusion. We also used the eTICI score as a measure of distal embolization. The eTICI score ranges from 0 (no antegrade reperfusion of the occluded vascular territory) to 3 (complete antegrade reperfusion). The eTICI score includes grade 2C (slow flow in a few distal cortical vessels or presence of small distal cortical emboli, corresponding to 90-99% reperfusion). To reach an eTICI score of 2B or higher, complete DSA runs including anteroposterior and lateral views after EVT were mandatory. If a lateral view was missing, 2A was the highest possible score. Successful reperfusion was defined as eTICI 2B-3.

Relevant imaging datasets (baseline non-contrast CT (NCCT), baseline CT Angiography (CTA), interventional Digital Subtraction Angiography (DSA), and follow up imaging, if applicable) were collected, anonymized, stored in an imaging database (XNAT; NRG, St. Louis, Missouri, USA), and subsequently analysed by an imaging core lab. Observers were blinded to all clinical findings, with exception of clinical assessment of lesion location in the case of baseline NCCT. In separate sessions, the core lab evaluated ASPECT score on baseline CT, eTICI on DSA, and presence of intracranial haemorrhage on follow up CT.

Complications that occurred during intervention, hospital admittance, or in the 3-month follow up period were registered and evaluated by the serious adverse event (SAE) committee. Medical records were searched for complications to prevent underreporting. These included intracranial haemorrhage, progression of ischemic stroke (resulting in a decline of at least 4 points on the NIHSS), new ischemic stroke, extracranial haemorrhage, and death.

Intracranial haemorrhage on follow up imaging was classified according to the Heidelberg criteria[18] and was considered symptomatic if the patient had died or had deteriorated neurologically (a decline of at least 4 points on the NIHSS), and the haemorrhage was related to the clinical deterioration (according to Heidelberg criteria). Symptomatic intracranial haemorrhage (sICH) was assessed by the SAE committee after evaluation of medical reports and imaging assessment.

Treatment

Patients were treated according to national guidelines for treatment of acute ischemic stroke, including intravenous thrombolysis if indicated.[17] Choice of clot retriever method was left to the attending physician's preference. Direct aspiration was defined as aspiration with a syringe or mechanical pump on a large bore catheter near the occluding clot.

Anaesthetic management varied depending on local protocols. In most centres patients were treated primarily with local anaesthetics only. In two hospitals, general anaesthesia was applied in almost all patients. In two centres general anaesthesia and local anaesthesia were used equally.

Statistical analyses

Baseline characteristics are presented in a descriptive way as mean and standard deviation (SD), median and interquartile range (IQR), or frequency (%), and compared between patients who underwent first treatment with aspiration versus stent retriever thrombectomy. Differences between the groups were tested with Pearsons chi-square test in case of ordinal/nominal variables. All data sets with continuous variables were checked for normality of distribution using a normal probability plot and the Kolmogorov-Smirnov test. For comparison of continuous variables we used the unpaired T-test combined with Levene's test

to check for homogeneity. If the distribution was not normal, we used the Mann-Whitney-U test. The level of significance was set at 0.05.

Multivariable ordinal regression analyses were performed to identify factors predictive for clinical outcome (mRS) at 3 months. Potential factors that were included in this analysis were determined based on (i) any (clinical) significant group difference in the comparison of baseline characteristics and (ii) factors known to influence outcome such as baseline NIHSS score and pre-stroke mRS score. Relations were expressed as odds ratios with corresponding 95% confidence intervals. We conducted a correlation analysis, calculating the Spearman rho on the independent variables before performing the ordinal regression analyses to prevent a misinterpretation of the results caused by multicollinearity.

Missing values

Missing NIHSS scores were retrospectively scored with a standardized score chart based on information from the reported neurological examination. If successful reperfusion was not achieved during EVT, the time of last contrast bolus injection was used as a proxy for time of duration of the procedure. Any mRS score of 0 to 5 assessed within 30 days was considered not valid and treated as missing. These values were therefore replaced by mRS scores derived from multiple imputation.[19] All descriptive analyses include all patients without imputation of the data. In order to make unbiased estimates of associations between intervention and outcome, multiple imputation was performed with the following variables: age, sex, baseline NIHSS score, diabetes mellitus, previous myocardial infarction, previous stroke, pre-stroke mRS score, atrial fibrillation, intravenous thrombolysis prior to EVT, systolic blood pressure, baseline ASPECTS, occlusion segment, CTA collateral status, time from symptom onset to

start of EVT, time from symptom onset to successful reperfusion, eTICI score at the end of the intervention, and NIHSS score after 24-48 hours.

All analyses were performed with SPSS 24 for Macintosh.

Results

In the MR CLEAN registry, 1628 patients have been registered between March 16, 2014 and June 15, 2016. For this analysis, 453 patients were excluded. Most of these (201) underwent catheterization only and no thrombectomy was performed, either because the target occlusion resolved, or due to distal migration of the clot. Another 45 underwent primary treatment other than by aspiration or stent retriever and were also excluded; in 67 patients, it was unclear which treatment method was used. The remaining 1175 patients were included, of whom 968 were initially treated with stent retriever and 207 with aspiration (Figure 1).

One of the sixteen intervention centres used aspiration as first-line strategy in most of the cases. In twelve centres stent retriever was the main first-line treatment modality. Three centres used both methods as initial approach equally.

Baseline characteristics

Pre-stroke mRS was higher in the aspiration group, and patients in the aspiration group more often underwent general anaesthesia (54% vs 24%, $p<0.05$). Level of occlusion differed significantly; patients in the aspiration group had a more distal occlusion site. Balloon guiding was used less in the aspiration group. The distribution of other baseline characteristics was similar in both groups (Table 1).

Table 1. Baseline characteristics of patients treated with aspiration or stent retriever.

	Aspiration N= 207	Stent retriever N= 968	P value
Demographics			
Age, median (IQR)	68.50 (54-77)	69 (57-78)	0.50
Male, n (%)	112 (54)	516 (53)	0.89
NIHSS baseline, median (IQR)	16 (12-21)	16 (12-19)	0.59
Pre-stroke mRS, n (%)			0.02
0	119 (59)	663 (70)	
1	29 (14)	116 (12)	
2	24 (12)	64 (7)	
>2	29 (14)	110 (12)	
Medical history, n (%)			
Previous stroke	31 (15)	162 (17)	0.62
Myocardial infarction	37 (19)	151 (16)	0.39
Peripheral arterial disease	17 (9)	85 (9)	0.99
Atrial fibrillation	38 (19)	224 (23)	0.21
Cardiovascular risk factors, n (%)			
Hypertension	99 (48)	495 (52)	0.33
Hypercholesterolemia	67 (34)	279 (30)	0.32
Diabetes mellitus	27 (13)	168 (18)	0.15
Smoking	47 (23)	226 (24)	0.97
Medication, n (%)			
Antiplatelet use	77 (38)	313 (33)	0.19

Coumadin	20	(10)	137	(14)	0.10
Statin	68	(34)	346	(37)	0.46
Stroke characteristics, n (%)					
IVT	156	(75)	741	(77)	0.73
Level of occlusion					0.02
ICA intracranial	51	(25)	272	(28)	
M1proximal	51	(25)	246	(26)	
M1distal	56	(29)	309	(33)	
M2	29	(15)	96	(10)	
M3	3	(2)	6	(1)	
A1	0	(0)	2	(0.2)	
A2	1	(0.5)	1	(0.1)	
ASPECTS subgroups,					0.91
0-4	12	(6)	64	(7)	
5-7	50	(25)	235	(25)	
8-10	137	(69)	633	(68)	
Collaterals					0.83
Absent collaterals	11	(6)	66	(7)	
Filling <50% of occluded area	62	(33)	294	(32)	
>50% but less than 100%	83	(44)	360	(40)	
Filling 100% of the occluded area	32	(17)	188	(21)	
Workflow					
Transfer from primary stroke centre, n (%)	120	(58)	527	(54)	0.40
Onset to IVT, median (IQR)	25,5	(17-32)	24	(19-34)	0.92

Onset to groin (minutes), median (IQR)	180	(150-225)	195	(155-245)	0.57
Balloon guiding yes, n (%)	30	(25)	591	(72)	<0.0001
Local anaesthesia only, n (%)	74	(31)	621	(61)	<0.0001
Conscious sedation, n (%)	23	(15)	128	(15)	0.99
General anaesthesia, n (%)	110	(54)	219	(24)	<0.0001

Continuous data are presented as mean (SD) for normal distributed data or as median (IQR) for skewed data. P values indicate differences between patients treated with stent retriever and direct aspiration.

Missing values: NIHSS baseline: 26 (2%), pre-stroke mRS: 21 (2%), Previous stroke: 7 (0.6%), history MI; 20 (2%), history PAD; 25 (2%), history DM; 8 (0.7%), hypertension; 13 (1%), AF; 16 (1%), hypercholesterolemia: 39 (3%), smoking: 276 (24%), antiplatelet therapy: 14 (1%), Coumadin use: 8 (0.7%), statin: 25 (2%), IVT: 3 (0.3 %), level of occlusion: 52 (4%), ASPECTS: 44 (4%), collateral score: 79 (7%), conscious sedation: 175 (15%), general anaesthesia; 54 (3.5%), balloon guiding: >100.

Time onset to IVT: 524 (45%), duration ER intervention hospital to groin: 366 (31%).

Abbreviations: IQR, interquartile range; NIHSS, National Institute of Health Stroke Scale; mRS, modified Rankin Scale; IVT, intravenous thrombolysis; ICA, internal carotid artery; M(segment), middle cerebral artery; A(segment), middle cerebral artery; ASPECTS, Alberta Stroke Program Early CT Score; ER, emergency room; EVT, endovascular treatment.

Functional outcome

There was no significant difference in the distribution of the mRS between the treatment groups, with a common odds ratio (cOR) for a shift of at least 1-point improvement on the mRS after treatment with aspiration first of 0.962 (95% CI 0.73 -1.28). Adjustment for age,

intervention centre, collateral status, time from onset to groin, general anaesthesia, pre-stroke mRS and baseline NIHSS score did not change this significantly (acOR 1.020 (95% CI 0.68-1.52)), (Figure 2).

Technical outcome

Successful reperfusion (eTICI ≥2B) was achieved slightly more often, although not significantly, in the aspiration group than in the stent retriever group (63% vs 56%; p=0.06). Duration of the endovascular procedure was shorter in the aspiration group: median 57 minutes (IQR 35-73) vs. median 70 minutes (IQR 47-95, p= <0.0001, Table 2).

Table 2. Outcomes, complications

	Aspiration N=207	Stent retriever N=968	P value
Duration of procedure in minutes, median (IQR)	56,5 (35-73)	70 (47-95)	<0.0001
ER first hospital to reperfusion in minutes/last contrast bolus, median (IQR)	164 (137-232)	196 (151-245)	<0.0001
SAE any, n (%)	85 (41)	414 (43)	0.71
Intracranial haemorrhage total, n (%)	18 (9)	55 (6)	0.14
sICH periprocedural	5 (28)	16 (30)	
sICH after 24h	9 (50)	30 (56)	
sICH after 48h	3 (17)	2 (4)	
sICH at discharge	1 (6)	4 (7)	

sICH at follow-up	0	(0)	2	(4)	
Post EVT eTICI, n (%)					0.03
0	28	(14)	128	(13)	
1	1	(1)	44	(5)	
2A	46	(22)	250	(26)	
2B	33	(16)	174	(18)	
2C	24	(12)	85	(9)	
3	70	(35)	271	(29)	
Successful reperfusion (eTICI 2B-3), n (%)	127	(63)	530	(56)	0.06
NIHSS 12-48 hour, median (IQR)	12	(4-18)	11	(4-17)	0.60
mRS 3 months follow-up, n (%)					0.72
0	9	(5)	47	(5)	
1	19	(11)	113	(13)	
2	41	(23)	175	(20)	
>2	111	(62)	560	(63)	
Stroke progression resulting in neurodetoriation/death, n (%)	17	(8)	101	(10)	0.40
New ischemic stroke resulting in neurodetoriation/death, n (%)	5	(2)	16	(2)	0.64
Mortality, n (%)	56	(27)	256	(26)	0.93
Mortality within 7 days	27	(13)	137	(14)	0.76
Mortality within 1 month	45	(22)	213	(22)	1.00

Missing values: Time onset- reperfusion: 35 (0.3%), Time duration of procedure: 80 (7%), Moment of sICH: 1, Post EVT eTICI: 21 (2%), NIHSS 12-48 hours: 119 (10%), mRS 3 months follow-up: 100 (9%).

Abbreviations: IQR, interquartile range; ER, emergency room; SAE, serious adverse events; eTICI, extended Thrombolysis in Cerebral Infarction; sICH, symptomatic intracranial haemorrhage; NIHSS, National Institute of Health Stroke Scale; mRS, modified Rankin Scale.

Safety

sICH was seen in 18 patients (9%) in the aspiration group, vs. 55 (6%) in the stent retriever group (p = 0.14). Mortality did not differ significantly between both groups (27 % in the aspiration group vs. 26 % in the stent retriever group (p = 0.93), Table 2)

Clinically significant new infarction occurred in 5 patients (2%) in the aspiration group vs. 16 (2%) in the stent retriever group (p = 0.64). Distal embolization rates seemed the same in both groups, as reperfusion rates (especially eTICI 2B and 2C scores) were the same.

First line strategy only

Single pass successful reperfusion was achieved in 108 patients (52%) with aspiration and in 458 (47%) with stent retriever thrombectomy (p = 0.53). If successful reperfusion was achieved after a single pass, median time of EVT was 40 (IQR 30-60) minutes with aspiration vs. 52 (IQR 35-75) minutes with stent retriever (p < 0.001).

Single pass successful reperfusion rate was highest in case of a proximal M1 occlusion (70% with aspiration vs. 59% with stent retriever, p = 0.13) and lowest in case of an intracranial ICA occlusion (31% with aspiration vs. 30% with stent retriever p = 0.18).

Fifteen patients (3%) had a periprocedural sICH after single pass with stent retriever vs. 1 (0.9%) with aspiration (p= 0.15).

Additional treatment

An additional attempt after first line strategy was performed in 45 patients (22%) in the aspiration group, and 248 (26%) in the stent retriever group (Figure 1). In the stent retriever group, 107 patients (11%) were converted to aspiration, of whom 52% achieved successful reperfusion. In the aspiration group 35 patients (17%) were converted to stent retriever treatment, in which 15 patients (43%) achieved successful reperfusion. For the second, third and fourth attempts, either aspiration or stent retriever were used, without differences between the groups. After these additional attempts, 26 (58%) patients achieved successful reperfusion in the aspiration group and 114 (46%) in the stent retriever group (p= 0.15).

Discussion

This study shows that in routine clinical practice similar technical and clinical results are achieved when EVT is performed by direct aspiration or stent retriever as first approach in patients with acute ischemic stroke due to large vessel occlusive stroke of the anterior circulation. The results of this large patient cohort are in line with those of earlier studies comparing the technical outcomes of these thrombectomy techniques and adds important results on clinical outcome.[11,12,14,16,20] Compared to RCTs our results more closely reflect the use of both techniques in daily clinical practice with patient selection according to current clinical guidelines. Both techniques were performed by experienced interventionalists, minimalizing learning curve effect.

Results of our study show equal reperfusion rates with a single pass of aspiration compared to stent retriever. However, aspiration showed shorter procedure times than thrombectomy by stent retriever. Consequently, the time from onset of symptoms to reperfusion was shorter in patients treated with aspiration. This finding is in line with the ASTER trial and reported but as of yet unpublished results of the COMPASS trial.

Although favourable clinical outcome is strongly associated with time to reperfusion[21], we did not observe a significant difference in functional outcome between patients treated with aspiration or stent retriever. The latter may be related to several factors: First, general anaesthesia was more often applied in the aspiration than in the stent retriever group (aspiration 54% vs stent retriever 24%) whereas local anaesthesia was the most commonly used method in the stent retriever group (aspiration 31% vs stent retriever 61%). The role of type of anaesthesia on outcome remains unclear at this point. Although studies comparing general anaesthesia and conscious sedation in EVT showed equivalence, data comparing these two methods with local anaesthesia only are lacking.[22–25] Differences in general anaesthesia use are probably related to centre specific preferences.

Second, pre-stroke mRS was higher in the aspiration group. However, for both of the above-mentioned factors adjustment was applied in our analysis. More likely, the time difference between the two procedures may be too short and the groups too small to provide significant differences in functional recovery. In the stent retriever group, 107 patients (11%) were converted to aspiration, of whom 52% achieved successful reperfusion. In the aspiration group 35 patients (17%) were converted to stent retriever treatment, 15 patients (43%) achieved successful reperfusion. This indicates that conversion to the aspiration strategy may be advantageous, if first attempts with stent retriever are failing and vice versa.

The number of second passes for both techniques are in line with other studies.[16][20]

Safety

Intracranial haemorrhage may be caused by reperfusion injury or by device induced vessel damage. The latter may be caused by manipulation of the intracranial vasculature with any thrombectomy device.[13] We found no difference in the occurrence of intracranial bleeding between both groups.

A matter of concern in mechanical thrombectomy is the per procedural thrombus fragmentation leading to the spread of emboli in a previously uninvolved arterial territory.[26] We observed no differences with regard to clinically relevant infarction in another territory between the treatment groups. In addition, reperfusion rates were similar, especially eTICI 2B and 2C scores, indicating that both techniques probably induced same rates of thrombus fragmentation. This is in accordance with other studies.[16,27]

Limitations

This study is not a randomized clinical trial, however both groups had largely similar baseline characteristics and with this study design the results represent daily clinical practice in a large real life cohort. In this multicentre observational study not every centre used the same treatment protocols: for example anaesthetic management and choice of treatment modality varied. Significant differences in baseline characteristics (pre-stroke mRS, use of general anaesthesia, balloon guiding use, site of occlusion) seem to be less favourable for aspiration than stent retriever in our cohort, based on the current state of knowledge.

Giving procedures in which final lateral DSA is missing a maximum eTICI score of 2A potentially leads to underreporting of successful reperfusion, we assume this occurred at a similar frequency in both groups and this would not influence our results.

The combined treatment of stent retriever and aspiration could not be analysed separately; in this analysis it is considered a stent retriever approach.

Conclusion

The results of this large multicenter real life cohort study showed no difference in safety and outcome between direct aspiration and stent retriever thrombectomy as first line treatment strategy in acute stroke patients with a large vessel occlusion. Both approaches are equally effective in endovascular treatment of acute ischemic stroke. This study confirms in a real-life population what has been previously reported in randomized trials.

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Personal disclosures

None reported.

Medical ethic committee statement

The MR CLEAN Registry was approved by the ethics committee of the Erasmus University MC, Rotterdam, The Netherlands (MEC-2014-235). With this approval it was approved by the research board of each participating centre. At UMC Utrecht, approval to participate in the study has been obtained from their own ethics committee.

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Competing Interests Statement

We have read and understood BMJ policy on declaration of interests and declare that we have no competing interests.

Contributorship Statement

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ML-B wrote the statistical analysis plan, designed the first draft, conducted statistical analysis and revised draft paper.

RJ-G, JM and JH participated in study design, data collection, data analysis, interpretation, and writing of the manuscript.

RJ-G, JH, JM, WvZ, RvO, YR, MU revised draft paper.

The study coordinators, local investigators, and members of the executive, imaging, and complication committees collected the data,

All authors critically reviewed the manuscript and approved the final version.

Data sharing Statement

N/A

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Figure legends

Figure 1

Title: Flow of patients through this study.

Abbreviations: EVT, endovascular treatment; MR CLEAN, Multicentre Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; DSA, Digital Subtraction Angiography.

Figure 2

Title: Distribution of scores on the modified Rankin Scale for the aspiration and stent retriever groups.

Caption: There is no statistically significant difference between the groups in the overall distribution of scores in an analysis with univariable ordinal regression. There was no significant shift in the mRS distribution in favour of the aspiration strategy, with a cOR for a 1-point improvement of score on the mRS of 0.962 (95% CI 0.725 -1.276). Results after adjustment for age, intervention centre, collaterals, time to groin, National Institutes of Health Stroke Scale score at baseline, general anaesthesia and pre-stroke mRS in an analysis with multivariable regression are essentially the same (acOR 1.020 (95% CI 0.68-1.52)).

Abbreviations: mRS, modified Rankin Scale